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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,940	11/21/2001	Hui Tian	018781-007410US	2892

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EXAMINER	
KAUFMAN, CLAIRE M	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/990,940	TIAN ET AL.	
	Examiner	Art Unit	
	Claire M. Kaufman	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *3/1/04*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,18,23,49-51 and 55-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17,18,23,49-51 and 55-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

In view of the papers filed March 1, 2004, the inventorship in this nonprovisional application has been changed by the deletion Jiagang Zhao, Jin-Long Chen, Songzhu An, Kang Dai and Jamila S.

The Office of Initial Patent Examination (OIPE) has been notified to issue a corrected filing receipt, and correct PTO PALM data to reflect the inventorship as corrected.

The claims have been amended as set forth in the paper filed 3/1/04.

Information Disclosure Statement

Reference JP 2001-245666 has been considered as indicated on the attached PTO-892.

Response to Amendment

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection of claims 19-22, 24, 25, 31, 32 and 52-54 are moot in view of the cancellation of the claims.

The rejection of claims under 35 USC 112, second paragraph, is withdrawn in view of the amendment to or cancellation of the claims.

The rejection of claims under 35 USC 102 is withdrawn in view of the amendment to the claims and Applicants' arguments.

The Declaration under 37 CFR 1.132 filed March 1, 2004, is insufficient to overcome the rejection of claims 17, 18, 23, 49-51 and 55 and new claims 56-59 based upon 35 USC 101/112, first paragraph, as set forth in the last Office action because: as discussed below, increase in intracellular calcium by a peptide ligand which was not disclosed and confers no other known function to TGR346 other than intracellular calcium increase, an activity common to many

diverse receptors, does not support a specific and substantial utility or enablement as require under the statutes.

Specification

The disclosure is objected to because of the following informality: on p. 22, ¶91, there is no end parenthesis in the parenthetical phrase beginning on line 6.

Appropriate correction is required.

Claim Rejections - 35 USC § 101/112, First Paragraph

Claims 17, 18, 23, 49-51 and 55 remain and new claims 56-59 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth in the previous Office action (mailed 10/02/03) on pages 5-6.

Claims 17, 18, 23, 49-51 and 55 remain and new claims 56-59 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention for the reasons set forth in the previous Office action (mailed 10/02/03) on pages 6-7.

Applicants argue (pp. 7-9 of REMARKS) the claimed nucleic acid meets the requirements of 35 U.S.C. 101 because identification of the TGR346 nucleic acids permits one of skill in the art to, for example, screen for agonists or antagonists of TGR346 activity, which can be used, e.g., for modulating TGR346 activity in brain cells. The argument has been fully considered, but is not persuasive. Use of TGR346 as a research tool, such as in a method to identify an agonist, provides an invitation to experiment to find a specific and substantial use for the claimed invention. Any orphan receptor may serve in an assay to identify an agonist. As stated in the previous Office action in the middle of page 6:

> The above utilities are not specific or substantial because they are generally applicable to any receptor and there is no known particular function of the instantly claimed encoding nucleic acid. Additionally, it is not known if the nucleic acid or encoded protein are differentially expressed (*e.g.*, over- or under-expressed or mutated), and if such

expression would reasonably be expected to be associated with any known disease, so the asserted utility is not specific. If the encoded protein does not have utility because neither its function nor a directly associated disease is known, then antibodies that bind the encoded protein do not utility. Because it is not known specifically what the functional properties of the polypeptide encoded by the claimed nucleic acid are or what specific properties aside from sequence (*e.g.*, differential expression) the claimed nucleic acid or protein has, the claimed invention is not supported by a substantial, specific or well established utility.

Applicants argue (p. 8) that as a GPCR, TGR346 has utility as a functional GPCR as supported by the Declaration which presents data showing that murine TGR346b, which is encoded by SEQ ID NO:17, has a known G-protein coupled receptor activity, i.e.., it transduces an increase in intracellular calcium, with GPCR activity assayable using a variety of common assays. The argument has been fully considered, but is not persuasive. The diversity of activities and modes of action are so great for the GPCR family that to say that a protein is a member does not provide a specific utility (*e.g.*, serotonin receptor compared to rhodopsin photosensitive receptor having specific recognized utilities/functions). The use of an orphan receptor to identify ligands is not specific but is instead a hunting expedition to determine a function or specificity of the receptor. The claims are not restricted generically to the whole family of GPCRs but to particular encoded sequences with unknown functional properties.

Applicants argue (p. 9) that the claimed invention has a "real world" use for identifying modulators of brain cell physiology. The argument has been fully considered, but is not persuasive. Until some actual and specific significance can be attributed to TGR346 or the nucleic acid encoding it, one of skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility as of the filing date.

Applicants argue that utility is credible (p. 9). Credibility is not at issue here. However, the transduction of an intracellular calcium change is credible, if not specific or substantial.

Applicants argue (pp. 9-10) that the instant invention is beneficial to the public as a means of screening for TGR346 modulators, citing *Nelson v. Bowler* (CCPA 1980). The argument has been fully considered, but is not persuasive. The instant situation is distinguished from *Nelson* because in *Nelson*, the pharmaceutical was known and described and had disclosed

properties recognized as more likely than not conferring therapeutic benefit (blood pressure change and smooth muscle stimulation) that the skilled artisan would be able to take advantage of without undue experimentation. On the contrary, in the instant situation, no modulator is known or described. No therapeutic benefits can be specifically attributed to the receptor that is described. A means of screaning for a modulator is an invitation to experiment without a reasonable expectation of successfully obtaining a modulator with therapeutic properties that would make it beneficial to the public. In *Brenner v. Manson* 148 U.S.P.Q. 689 (1966), cited by Applicants, a novel compound which was structurally analogous to other compounds which were known to possess anti-tumor activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court held that:

> The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. . . . [u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. . . . a patent is not a hunting license. . . .[i]t is not a reward for the search, but compensation for its successful conclusion.

As set forth in the original rejection, it is maintained as discussed above that the claimed nucleic acid does not have utility under the requirements of 35 USC 101 and 112, first paragraph.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Claire M. Kaufman, whose telephone number is (571)272-0873. Dr. Kaufman can generally be reached Monday, Tuesday and Thursday from 8:30AM to 2:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached at (571)272-0871.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (571) 272-1600.

Official papers filed by fax should be directed to (703) 872-9306. NOTE: If applicant *does* submit a paper by fax, the original signed copy should be retained by the applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Claire M. Kaufman, Ph.D.

Patent Examiner, Art Unit 1646

June 7, 2004

LORRAINE SPECTOR
PRIMARY EXAMINER